IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	**MDL Docket No. 4:03CV1507 WRW**
PREMPRO PRODUCTS LIABILITY LITIGATION	***Reeves v. Wyeth,* 4:05-cv-00163-WRW** ***Rush v. Wyeth, et al.*, 4:05-cv-00497-WRW**

No. 8

MEMORANDUM IN SUPPORT OF DEFENDANTS' MOTION TO EXCLUDE EXPERT TESTIMONY OF DR. GRAHAM A. COLDITZ

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After purportedly summarizing the "[o]verall benefits and harms of combination hormone replacement therapy," Dr. Colditz declares that "the weight of evidence is overwhelmingly against long-term use of exogenous menopausal hormone therapy and that even short term use, which still carries harms, should be as a last resort for women with severe menopausal symptoms."[1] Dr. Colditz acknowledged, however, that his conclusion was not derived from a "rigorous, complete, risk/benefit analysis" based on a "scientific synthesis of evidence."[2] His "methodology" therefore fails to comport with the requirements of *Daubert*,[3] and fails to have any relevance to the issues the jury must resolve in these bellwether cases.

The Court should exclude his overall risk/benefit opinions[4] for two reasons.

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1 Report of Dr. Graham A. Colditz ("Colditz Rep.") (App., Ex. 8) at 1.

2 Deposition of Dr. Graham A. Colditz (May 2, 2006) ("Colditz Dep.") (App., Ex. 7) at 336:6-12; 395:14-17.

3 *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 479 (1993).

4 These opinions support Plaintiffs' design defect claim. Because Wyeth is entitled to summary judgment on that claim for the reasons given in Wyeth's Memorandum No. 1 (in Support of Motion for Partial Summary Judgment Re Specific Claims) [Rush Docket No. 91; Reeves Docket No. 62], the Court need never reach this motion.

First, Dr. Colditz testified he will not offer any opinion about the adequacy of Wyeth's labeling in these cases or about causation in any individual case.[5] His musings about risk and benefit in the abstract therefore will not help jurors decide the concrete questions put to them, and will serve only to confuse them and unfairly prejudice Wyeth. Second, Dr. Colditz's opinions about risk/benefit fail to satisfy the requirements of *Daubert*. He admitted that his opinions did not reflect a "rigorous, complete, risk/benefit analysis" based on "a scientific synthesis of evidence,"[6] and that the "methodology" he employed could not possibly answer the question he was attempting to address.

ARGUMENT

I. DR. COLDITZ'S RISK/BENEFIT OPINIONS ARE IRRELEVANT TO ANY ISSUE IN THESE CASES.

The Federal Rules of Evidence are "designed not for the exhaustive search for cosmic understanding but for the particularized resolution of legal disputes."[7] Expert testimony must be relevant to the case at hand.[8] The Court's role as a gatekeeper requires it to screen proposed expert testimony "***in light of the specific circumstances of the case*** to ensure that it is reliable ***and sufficiently relevant*** to assist the jury in resolving the factual disputes."[9]

Wyeth is not seeking to exclude Dr. Colditz's general causation testimony regarding breast cancer.

5 Colditz Dep. at 24:18-26:3; 273:3-7.

6 *Id*. at 336:6-12; 395:14-17.

7 *Daubert*, 509 U.S. at 597.

8 *Margolies v. McCleary, Inc.*, __ F.3d __, No. 05-2122, 05-2123, 2006 WL 1359669, at *3 (8th Cir. May 19, 2006) ("In order to be admissible, expert testimony must be both relevant to a material issue and reliable.").

9 *Miller v. Baker Implement Co.*, 439 F.3d 407, 412 (8th Cir. 2006) (emphasis added).

Dr. Colditz's risk/benefit opinions fail the relevancy test. This Court is not hosting a symposium at which distinguished scientists will ponder issues in the abstract and lecture to the jury about the frontiers of science. It is not even presiding over a medical malpractice trial in which the wisdom of a doctor's risk/benefit decision for a particular patient is at issue, though Dr. Colditz's abstract opinions would be of little help there anyway. This is a product liability lawsuit in which the jury will have to decide: (1) whether hormone therapy caused the Plaintiffs' breast cancer; (2) if so, whether Wyeth provided an adequate warning to their doctors at the relevant time; and (3) if Wyeth did not, whether an "adequate" warning would have changed the doctors' prescribing decisions.

Dr. Colditz's risk/benefit opinions shed no light on any of these questions. The first question addresses specific causation, and Dr. Colditz concedes he has nothing to offer there: "We [epidemiologists] do not attribute cause at the individual level."[10] The second question addresses the adequacy of Wyeth's warnings, and Dr. Colditz explicitly disclaims any intent to opine on that issue.[11] The third question addresses whether the prescribing doctors would have done things differently had they seen different warnings, a question only those doctors can answer.

At bottom, all Dr. Colditz provides are conclusory sound bites (*e.g.,* "long-term combined hormone therapy ***should not be used***" and "even short-term use . . . should be as ***a last***

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[10] Colditz Dep. at 78:22-23.

[11] *Id*. at 273:3-7. Plaintiffs cannot use Dr. Colditz to support their inadequate warning claims because he offers no opinions about what risks and benefits were known (or knowable) in 1989-1990, when Ms. Reeves and Ms. Rush were first prescribed the hormone therapy. The vast majority of his 86 references are to literature published later than 1990; many are dated 2004 and later. Colditz Rep. at 11-15. Plaintiffs concede that the 2005 labeling for the drugs is adequate. Transcript of May 12, 2006 Status Conference [Docket No. 1182] at 94:11-17; 95:14-19 (excerpts attached as Ex. 64).

resort"),[12] that are probative of no issue the jury will consider.[13] His testimony on these issues does not help the jury "understand the evidence" or "determine a fact in issue" under Rule 702. Even if they were based on a reliable foundation (and they are not, as explained below), Dr. Colditz's free-floating risk/benefit opinions do not have a "tendency to make the existence of any fact that is of consequence to the determination of the action more probable or less probable than it would be without [those opinions]" under Rule 401. Instead, Dr. Colditz's broad-brush denigration of hormone therapy threatens to confuse the jury and unfairly prejudice Wyeth within the meaning of Rule 403 by suggesting to jurors that they are supposed to decide whether hormone therapy generally is a good or a bad thing instead of answering the specific liability questions the Court submits to them.

II. DR. COLDITZ'S "METHODOLOGY" DOES NOT COMPLY WITH THE REQUIREMENTS OF DAUBERT.

In *Daubert*, the Supreme Court explained that expert scientific testimony admitted under Rule 702 must possess "a grounding in the methods and procedures of science" and must be based on genuine knowledge; that is, "more than subjective belief or unsupported speculation."[14] Thus, "in order to qualify as 'scientific knowledge,' an inference or assertion must be derived by the scientific method."[15] In practical terms, an expert "may not reach his conclusion first and do

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[12] Colditz Rep. at 11:1 (emphasis added).

[13] Even if Dr. Colditz's risk/benefit opinions bore on a fact at issue, his concessions about the limits of those opinions (*i.e.*, hormone therapy should not be used more than two years—that is, unless a prescribing doctor weighing the risks and benefits for an actual patient decides otherwise) render them meaningless and unhelpful to the jury. *Cf. Pipitone v. Biomatrix, Inc.*, 288 F.3d 239, 245 (5th Cir. 2002) ("A perfectly equivocal opinion does not make any fact more or less probable and is irrelevant under the Federal Rules of Evidence.").

[14] *Daubert*, 509 U.S. at 589-90.

[15] *Id.* at 590.

the research later."[16] He must use the same rigor in the courtroom that he would apply in his non-litigation, scientific endeavors.[17]

Dr. Colditz's risk/benefit opinions do not make the grade.

A. Dr. Colditz Concedes that the Methodology He Employed Cannot Answer the Question He Poses.

Although Dr. Colditz applies epidemiological principles to attempt to sum up the risks versus benefits of hormone therapy, he ultimately concedes that such an endeavor is doomed to fail, since that determination can only be made on an individualized basis, between doctor and patient. And since Dr. Colditz, although a medical doctor, has "practiced the art of epidemiology" rather than "the art of hands-on clinical medicine" for the past twenty years,[18] he has no basis, and has made no attempt, to render such an opinion for either Mrs. Reeves or Mrs. Rush.

When he is writing as a scientist for his peers, Dr. Colditz admits that epidemiology provides information about risks at a broad population level, but tells us little about any one individual's risk:

> The words 'cause' and 'prevent,' as they pertain to probabilistic risk factor logic are concepts mostly clearly applied to aggregates of individuals, ***not a specific individual***. . . .[D]isease pathogenesis at the individual level is a very complex process. The misleading message that an individual can prevent a particular disease by altering a particular behavior or exposure (and its converse, ***that an***

[16] *In re Rezulin Prods. Liab. Litig.*, 309 F. Supp. 2d 531, 550 (S.D.N.Y. 2004).

[17] *Id.* at 563 (citing *Kumho Tire Co. Ltd. v. Carmichael*, 526 U.S. 137, 152 (1999)).

[18] Colditz Dep. at 36:8-11

> ***individual will develop a particular disease if such behavior is not changed***) has unfortunately been widely conveyed."[19]

At his deposition, too, Dr. Colditz acknowledged that epidemiology can identify increased risks in the aggregate, but does not "attribute cause at the individual level."[20] Accordingly, "[e]pidemiology doesn't spend its time looking at the cause in the individual."[21]

Most telling for this motion, Dr. Colditz conceded that an overall risk/benefit assessment is a determination that can ***only*** be made on an individualized basis, with the exercise of personalized clinical judgment:

> A: [T]he actual determination of where short-term/long-term is will come down to the individual doctor/patient discussion. It's not an absolute, thou can only use therapy for this number of months and then thou must stop.
>
> * * *
>
> Q: And do you agree that ultimately the decision about whether the risks of using hormone therapy, whether it's estrogen alone or combination therapy, outweigh the benefits is a decision to be left to an individual woman and her physician?
>
> A: ***Well, that is the ultimate tradeoff at the doctor/patient level to weigh the risks and benefits***. We can give as preventive services to overall guidance, but we need to consider the severity of menopausal symptoms, for example, their persistence, underlying risk of breast cancer, women with family history and so on, we may consider differently from women with no family history and so on.[22]

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[19] Colditz Dep. at 27:12-28:7; 28:21-29:9 (emphasis added) (quoting B. Rockhill, I Kawachi, and G.A. Colditz, *Individual Risk Prediction and Population-Wide Disease Prevention* 22 Epidemiological Reviews 176-180 (2000)).

[20] *Id*. at 26:1-3.

[21] *Id.* at 37:16-18.

[22] *Id.* at 350:21-351:3; 404:20-405:13 (emphasis added). *See also id.* at 339 (explaining that he did not attempt to place different weights on different outcomes [*i.e.*, comparing the value of certain benefits of hormone therapy with the value of certain risks of hormone therapy]

The bottom line? Dr. Colditz admits that, while the methods of epidemiology can provide general guidance on the issue, the ultimate determination of whether the risks of hormone therapy outweigh the benefits must be made on a case-by-case basis, between doctor and patient—something he has not attempted to do for Mrs. Reeves and Mrs. Rush (and something he would not do because he does not see or treat patients).[23]

B. Dr. Colditz's "Methodology" Is Unreliable and Unscientific by His Own Admission.

Whatever his methodology, we have Dr. Colditz's word for it that it is unreliable. By way of excusing his seemingly haphazard approach to selecting and weighing risks and benefits, Dr. Colditz repeatedly emphasized that his opinion was not intended to be a rigorous scientific assessment of the evidence:

> But I've not tried to—again, in a ***rigorous, complete, risk/benefit analysis,*** one will go out and do surveys of the value people place on all the different endpoints. ***We're not doing that here***. We're giving my best synthesis of the evidence and my opinion based on a review of the scientific evidence.[24]

One can only assume that Dr. Colditz considers a ***non***-rigorous, ***in***complete analysis "good enough" for the courtroom. Indeed, he basically says so:

> A: This is ***not a scientific synthesis of evidence*** across the totality of evidence.
>
> Q: And you're referring to your report now, correct?
>
> A: Absolutely, yes.[25]

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because "in some aspects of this clinical decision making, the sense is it should be much more—an issue that, if provided, discusses with individual women, because they will place different conditions as more or less important for them").

[23] *Id*. at 36:8-11.

[24] *Id.* at 336:6-15 (emphasis added).

[25] *Id.* at 395:14-21 (emphasis added).

If it is not a "scientific synthesis of evidence," why should the jury be permitted to hear about it from the mouth of someone cloaked in the mantle of an expert? It is axiomatic that an expert must employ "in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field."[26] Dr. Colditz, by his own admission, failed to satisfy this foundational requirement.

The fact that Dr. Colditz did not perform a rigorous, complete, analysis of risks and benefits is proven by the fact that Dr. Colditz did not consider a complete list of the benefits of hormone therapy. He offered no explanation for excluding from consideration altogether at least two potential benefits of hormone therapy—reduction in macular degeneration and reduction in the risk of new onset diabetes, although he considered other potential benefits not contained in the label.[27] He also relied on risk/benefit assessments by others that he knew to be incomplete or inaccurate. He relied, for example, on the WHI Global Index and the U.S. Preventive Services Task Force ("U.S.P.S.T.F.") statements despite knowing that both were based on the preliminary (rather than final) WHI data.[28] He made no effort to recalculate the Global Index using the final data.[29] And he relied on the WHI Global Index, the U.S.P.S.T.F., and Canadian Task Force statements about risk/benefit, knowing that these sources did not even attempt to factor in the principal benefit of relieving menopausal symptoms.[30]

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[26] *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999).

[27] Colditz Dep. at 391:17-394:2.

[28] *Id.* at 341:14-342:8; 344:23-345:3.

[29] *Id.* at 343:18-22.

[30] *Id.* at 347:2-348:24.

C. Dr. Colditz's Method Has Been Tested, and Failed.

The ability to validate a theory through testing is a cornerstone of the scientific method and, accordingly, of the reliability inquiry under *Daubert*:

> [A] key question to be answered in determining whether a theory or technique is scientific knowledge that will assist the trier of fact will be whether it can be (and has been) tested. "Scientific methodology today is based on generating hypotheses and testing them to see if they can be falsified; indeed, this methodology is what distinguishes science from other fields of human inquiry."[31]

Dr. Colditz testified that studying overall mortality in users versus non-users of hormone therapy is one way to make a risk/benefit assessment:

> Q: Would you agree that one way to test the overall risks and benefits of a therapy would be to assess whether mortality from that therapy is increased or decreased?
>
> A: ***One of the ways that we can assess the impact is to look at total mortality***. There are strengths and limitations in that endpoint as with many others, given that some conditions one can have and live with for a long time, others may be rapidly fatal, but ***it does give us a summary of risks and benefits, yes***."[32]

Yet he ultimately admitted (after attempting repeatedly to avoid the question) that the evidence shows either reduced mortality in hormone therapy users (*i.e.*, a net ***benefit***) or, at worst, no increase in mortality in hormone therapy users (a null effect).[33] None of the available evidence evaluating overall mortality supports Dr. Colditz's contention that the risks on balance outweigh

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[31] *Daubert*, 509 U.S. at 593 (quoting E. Green & C. Nesson, Problems, Cases, and Materials on Evidence 645 (1983)).

[32] Colditz Dep. at 381:14-382:3 (emphasis added).

[33] *Id.* at 381:14-21; 385:3-387:10.

the benefits. That he made no effort to reconcile this fact with the conclusion in his report condemns his analysis under *Daubert*.[34]

D. Dr. Colditz Selected Literature that Supported His Preconceived Opinion About Long-Term Use of Hormone Therapy—Something He Would Not Do Outside Litigation.

At the outset, Dr. Colditz commits two cardinal sins against the scientific method: (1) he works backwards from a predetermined conclusion,[35] and (2) he uses a less stringent standard for his litigation opinions than he would if he were writing for his peers:[36]

> Q: . . . And if you were doing a systematic review, you would, if publishing it look at all of the available evidence and attempt to explain that evidence which is inconsistent with your interpretation, correct?
>
> A: If I was doing a systematic review with a clearly defined focus for that review, absolutely, I would be addressing all the evidence on that focused question.
>
> Q: And would you agree with me that you have the same obligation coming into court in this case to acknowledge when there's evidence inconsistent with your view and to attempt to explain it?
>
> A: I don't agree with that. In the full context of putting my report together, I gave reference to ***representative studies that support the position I'm taking based on my overall knowledge of the scientific literature.***[37]

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[34] *Caraker v. Sandoz Pharm. Corp.*, 172 F. Supp. 2d 1046, 1049 (S.D. Ill. 2001) ("This Court rejects the plaintiffs' experts opinions inasmuch as they rely on selective data from epidemiological studies."); *see also Rutigliano v. Valley Bus. Forms*, 929 F. Supp. 779, 790 (D.N.J. 1996) (noting the lack of "any support for a diagnostic method that accepts only results that support a specific conclusion").

[35] "Coming to a firm conclusion first and then doing research to support it is the antithesis of the [scientific] method." *Claar v. Burlington N.R.R. Co.*, 29 F.3d 499, 502-03 (9th Cir. 1994); *see also Sorensen v. Shaklee Corp.*, 31 F.3d 638, 649 (8th Cir. 1994) (rejecting proffered scientific testimony based on backward reasoning).

[36] *Kumho Tire Co.*, 526 U.S. at 152.

[37] Colditz Dep. at 277:18-278:21 (emphasis added).

Dr. Colditz's admission that he failed to adhere to the same standards he would use in non-litigation work[38] is by itself enough to exclude his opinions as scientifically unreliable. That he apparently did so to support a predetermined opinion—or, said differently, to serve as an advocate—is further reason why his opinion should be excluded.[39]

CONCLUSION

The proposed testimony of Dr. Colditz is not only unscientific, it has nothing to do with any issue in this case. The Court should accordingly grant Wyeth's Motion To Exclude the Testimony of Dr. Graham A. Colditz.

Respectfully submitted,

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[38] *In re Rezulin*, 309 F. Supp. 2d at 563 (*citing Kumho Tire Co.*, 526 U.S. at 152).

[39] *Id.* at 550; *Wills v. Amerada Hess Corp.*, No. 98-7126, 2002 U.S. Dist. LEXIS 1546, at *29 (S.D.N.Y. Jan. 31, 2002), *aff'd*, 379 F.3d 32 (2d Cir. 2004).

CERTIFICATE OF SERVICE

I hereby certify that on this 5th day of June 2006 a true and correct copy of the foregoing Memorandum In Support of Defendants' Motion to Exclude Expert Testimony of Dr. Graham A. Colditz was electronically filed with the Clerk of Court using the CM/ECF system and a true and correct copy was forwarded by e-mail and first-class mail, postage prepaid, to the parties listed below.

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